

What is claimed is:

1. A method of treating, preventing or ameliorating a disease or disorder associated with aberrant B Lymphocyte Stimulator (BLyS) or BLyS receptor expression or activity, comprising administering to an animal in which such treatment, prevention or amelioration is desired, a BLyS binding polypeptide in an amount effective to treat, prevent or ameliorate the disease or disorder.
2. The method of claim 1, wherein the disease or disorder is an immune system disease or disorder.
3. The method of claim 2, wherein the immune system disease or disorder is an autoimmune disease or disorder.
4. The method of claim 2, wherein the immune system disease or disorder is an immunodeficiency.
5. The method of claim 3, wherein the autoimmune disease or disorder is lupus.
6. The method of claim 1, wherein the disease or disorder is glomerular nephritis.
7. The method of claim 2, wherein the immune system disease or disorder is rheumatoid arthritis, multiple sclerosis, hypogammaglobulinemia or hypergammaglobulinemia.
8. The method of claim 2 wherein the immune system disease or disorder is graft vs. host disease.
9. The method of claim 2, wherein the immune system disease or disorder is a proliferative disease or disorder.
10. The method of claim 9, wherein the proliferative disorder is cancer.

11. The method of claim 1, wherein the disease or disorder is an infectious disease or disorder.

12. A method of treating, preventing, or ameliorating an immune system disease or disorder, comprising administering to an animal in which such treatment, prevention, or amelioration is desired, a BLYS binding polypeptide in an amount effective to treat, prevent, or ameliorate the immune system disease or disorder.

13. The method of claim 12, wherein the immune system disease or disorder is an autoimmune disease or disorder.

14. The method of claim 12, wherein the immune system disease or disorder is an immunodeficiency.

15. The method of claim 13, wherein the autoimmune disease or disorder is lupus.

16. The method of claim 12, wherein the immune system disease or disorder is glomerular nephritis, rheumatoid arthritis, multiple sclerosis, hypogammaglobulinemia, hypergammaglobulinemia, or graft vs. host disease.

17. A method of treating, preventing or ameliorating a disease or disorder of cells of hematopoietic origin, comprising administering to an animal in which such treatment, prevention, or amelioration is desired, a BLYS binding polypeptide in an amount effective to treat, prevent or ameliorate the disease or disorder.

18. The method of claim 17, wherein the cells of hematopoietic origin are selected from the group consisting of: lymphocytes, monocytes, macrophages, or dendritic cells.

19. The method of claim 18, wherein the lymphocytes are B cells.

20. The method of claim 18, wherein the lymphocytes are T cells.
21. A method of inhibiting or reducing immunoglobulin production, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide inhibits or reduces BLyS mediated immunoglobulin production.
22. The method of claim 21, wherein IgG production is inhibited or reduced.
23. The method of claim 21, wherein IgM production is inhibited or reduced.
24. The method of claim 21, wherein IgA production is inhibited or reduced.
25. A method of inhibiting or reducing immunoglobulin production, comprising administering to an animal in which such inhibition or reduction is desired, a BLyS binding polypeptide in an amount effective to inhibit or reduce immunoglobulin production.
26. The method of claim 25, wherein IgG production is inhibited or reduced.
27. The method of claim 25, wherein IgM production is inhibited or reduced.
28. The method of claim 25, wherein IgA production is inhibited or reduced.
29. A method of inhibiting or reducing B cell proliferation, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide inhibits or reduces BLyS mediated B cell proliferation.
30. A method of inhibiting or reducing B cell proliferation comprising administering to an animal in which such inhibition or reduction is desired, a BLyS binding polypeptide in an amount effective to inhibit or reduce B cell proliferation.

31. A method of inhibiting or reducing activation of B cells, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide inhibits or reduces BLyS mediated B cell activation.
32. A method of inhibiting or reducing activation of B cells, comprising administering to an animal in which such inhibition or reduction is desired, a BLyS binding polypeptide in an amount effective to inhibit or reduce B cell activation.
33. A method of decreasing lifespan of B cells, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide inhibits or reduces BLyS regulated lifespan of B cells.
34. A method of decreasing B cell lifespan, comprising administering to an animal in which such decrease is desired, a BLyS binding polypeptide in an amount effective to decrease B cell lifespan.
35. A method of inhibiting or reducing graft rejection, comprising administering to an animal in which such inhibition or reduction is desired, a BLyS binding polypeptide in an amount effective to inhibit or reduce graft rejection.
36. A method of killing cells of hematopoietic origin, comprising contacting BLyS binding polypeptides with BLyS to form a complex; and contacting the complex with cells of hematopoietic origin.
37. The method of ~~claim 36~~, wherein the cells of hematopoietic origin are selected from the group consisting of: lymphocytes, monocytes, macrophages, or dendritic cells.
38. The method of ~~claim 37~~, wherein the lymphocytes are B cells.
39. The method of ~~claim 37~~, wherein the lymphocytes are T cells.

40. A method of killing cells of hematopoietic origin, comprising administering to an animal in which such killing is desired, a BLyS binding polypeptide in an amount effective to kill cells of hematopoietic origin .

41. The method of claim 40, wherein the cells of hematopoietic origin are selected from the group consisting of: lymphocytes, monocytes, macrophages, or dendritic cells.

42. The method of claim 41, wherein the lymphocytes are B cells.

43. The method of claim 41, wherein the lymphocytes are T cells..

44. A method of treating a proliferative disease or disorder, comprising administering to an animal in which such treatment is desired, a BLyS binding polypeptide in an amount effective to treat the proliferative disease or disorder.

45. The method of claim 44, wherein the proliferative disease or disorder is selected from the group consisting of: premalignant conditions, benign tumors, hyperproliferative disorders, and benign proliferative disorders.

46. The method of claim 44, wherein the proliferative disease or disorder is a proliferative disease or disorder of a cell of hematopoietic origin.

47. The method of claim 46, wherein the proliferative disease or disorder is a B cell proliferative disease or disorder.

48. The method of claim 47, wherein the B cell proliferative disease or disorder is a leukemia.

49. The method of claim 47, wherein the B cell proliferative disease or disorder is a lymphoma.

50. The method of ~~claim 47~~, wherein the B cell proliferative disease or disorder is chronic lymphocytic leukemia, multiple myeloma, non-Hodgkin's lymphoma, or Hodgkins disease.

51. The method of ~~claim 46~~, wherein the proliferative disease or disorder is a T cell proliferative disease or disorder.

52. The method of ~~claim 46~~, wherein the proliferative disease or disorder is a monocytic proliferative disease or disorder.

53. The method of ~~claim 52~~, wherein the monocytic proliferative disease or disorder is leukemia, lymphoma, or acute myelogenous leukemia.

54. The method of ~~claim 46~~, wherein the proliferative disease or disorder is a macrophage proliferative disease or disorder.

55. A method of stimulating immunoglobulin production, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of the BLyS binding polypeptide stimulates BLyS mediated immunoglobulin production.

56. The method of ~~claim 55~~, wherein IgG production is stimulated.

57. The method of ~~claim 55~~, wherein IgM production is stimulated.

58. The method of ~~claim 55~~, wherein IgA production is stimulated.

59. A method of stimulating immunoglobulin production comprising administering to an animal in which such stimulation is desired, a BLyS binding polypeptide in an amount effective to stimulate immunoglobulin production.

60. The method of ~~claim 59~~, wherein IgG production is stimulated.

61. The method of claim 59, wherein IgM production is stimulated.
62. The method of claim 59, wherein IgA production is inhibited or stimulated.
63. A method of stimulating B cell proliferation, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide stimulates BLyS mediated B cell proliferation.
64. A method of stimulating B cell proliferation, comprising administering to an animal in which such stimulation is desired, a BLyS binding polypeptide in an amount effective to stimulate B cell proliferation.
65. A method of increasing activation of B cells, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide increases BLyS mediated activation of B cells.
66. A method of increasing activation of B cells, comprising administering to an animal in which such increase is desired, a BLyS binding polypeptide in an amount effective to increase B cell activation.
67. A method of increasing lifespan of B cells, comprising contacting an effective amount of BLyS binding polypeptide with BLyS, wherein the effective amount of BLyS binding polypeptide increases BLyS mediated lifespan of B cells.
68. A method increasing lifespan of B cells, comprising administering to an animal in which such increase is desired, a BLyS binding polypeptide in an amount effective to increase lifespan of B cells.
69. The method according to any one of claims 1, 12, 17, 21, ~~25~~, 29, 30, 31, 32, 33, 34, 35, 36, 40, 44, 55, 59, 63, 64, 65, 66, 67, or 68, wherein the BLyS binding polypeptide comprises an amino acid sequence selected from the group consisting of:

(1) Asp-Xaa-Leu-Thr (SEQ ID NO:446), where Xaa is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala (preferably Pro or Ser);

(2)  $X_1$ - $X_2$ - $X_3$ -Cys- $X_5$ -Phe- $X_7$ -Trp-Glu-Cys- $X_{11}$ - $X_{12}$ - $X_{13}$  (SEQ ID NO:1), wherein

5  $X_1$  is Ala, Asn, Lys, or Ser;

$X_2$  is Ala, Glu, Met, Ser, or Val;

$X_3$  is Ala, Asn, Lys, or Pro (preferably Lys);

$X_5$  is Phe, Trp, or Tyr (preferably Tyr);

$X_7$  is Pro or Tyr (preferably Pro);

10  $X_{11}$  is Ala, Gln, His, Phe, or Val;

$X_{12}$  is Asn, Gln, Gly, His, Ser, or Val; and

$X_{13}$  is Ala, Asn, Gly, Ile, Pro, or Ser;

(3)  $X_1$ - $X_2$ - $X_3$ -Cys- $X_5$ - $X_6$ - $X_7$ - $X_8$ - $X_9$ - $X_{10}$ -Cys- $X_{12}$ - $X_{13}$ - $X_{14}$  (SEQ ID NO:2), wherein

$X_1$  is Ala, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, Val, or is absent;

$X_2$  is Ala, Asn, Asp, Gln, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val;

$X_3$  is Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Trp, Tyr, or Val (preferably Asp);

20  $X_5$  is Asp, Ile, Leu, or Tyr (preferably Asp or Leu);

$X_6$  is Arg, Asp, Glu, His, Ile, Leu, Lys, Phe, Pro, Tyr, or Val (preferably Glu or Leu);

$X_7$  is His, Leu, Lys, or Phe (preferably His or Leu);

$X_8$  is Leu, Pro, or Thr (preferably Thr or Pro);

$X_9$  is Arg, Asn, Gly, His, Ile, Lys, Met, or Trp (preferably Lys);

25  $X_{10}$  is Ala, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Ser, Trp, Tyr, or Val;

$X_{12}$  is Asp, Gln, Glu, Gly, Ile, Leu, Lys, Phe, Ser, Trp, Tyr, or Val;

$X_{13}$  is Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val; and

$X_{14}$  is Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Phe, Pro, Trp, Tyr, Val, or is absent;

30 (4)  $X_1$ - $X_2$ - $X_3$ -Cys- $X_5$ - $X_6$ - $X_7$ - $X_8$ - $X_9$ - $X_{10}$ - $X_{11}$ -Cys- $X_{13}$ - $X_{14}$ - $X_{15}$  (SEQ ID NO:3), wherein



X<sub>1</sub> is Ala, Arg, Asn, Asp, Leu, Lys, Phe, Pro, Ser, or Thr;

X<sub>2</sub> is Asn, Asp, Gln, His, Ile, Lys, Pro, Thr, or Trp;

X<sub>3</sub> is Ala, Arg, Asn, Gln, Glu, His, Phe, Pro, or Thr (preferably Ala);

X<sub>5</sub> is Asn, Asp, Pro, Ser, or Thr (preferably Asp);

5 X<sub>6</sub> is Arg, Asp, Ile, Leu, Met, Pro, or Val (preferably Ile);

X<sub>7</sub> is Ala, Ile, Leu, Pro, Thr, or Val (preferably Val or Leu);

X<sub>8</sub> is Asn, His, Ile, Leu, Lys, Phe, or Thr (preferably Thr);

X<sub>9</sub> is Asn, Glu, Gly, His, Leu, Lys, Met, Pro, or Thr (preferably Leu);

X<sub>10</sub> is Arg, Asn, Asp, Gln, Glu, Gly, Ile, Lys, Met, Pro, Ser, or Trp;

10 X<sub>11</sub> is Arg, Glu, Gly, Lys, Phe, Ser, Trp, or Tyr (preferably Ser);

X<sub>13</sub> is Gln, Glu, Ile, Leu, Phe, Pro, Ser, Tyr, or Val (preferably Val);

X<sub>14</sub> is Asn, Gly, Ile, Phe, Pro, Thr, Trp, or Tyr; and

X<sub>15</sub> is Asn, Asp, Glu, Leu, Lys, Met, Pro, or Thr (preferably Glu or Pro);

(5) X<sub>1</sub>-X<sub>2</sub>-X<sub>3</sub>-Cys-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-X<sub>9</sub>-X<sub>10</sub>-X<sub>11</sub>-X<sub>12</sub>-Cys-X<sub>14</sub>-X<sub>15</sub>-X<sub>16</sub> (SEQ ID NO:4),

wherein

X<sub>1</sub> is Asn, Asp, His, Leu, Phe, Pro, Ser, Tyr, or is absent (preferably Ser);

X<sub>2</sub> is Arg, Asn, Asp, His, Phe, Ser, or Trp (preferably Arg);

X<sub>3</sub> is Asn, Asp, Leu, Pro, Ser, or Val (preferably Asn or Asp);

20 X<sub>5</sub> is Asp, Gln, His, Ile, Leu, Lys, Met, Phe, or Thr;

X<sub>6</sub> is His, Ile, Leu, Met, Phe, Pro, Trp, or Tyr;

X<sub>7</sub> is Asp, His, Leu, or Ser (preferably Asp);

X<sub>8</sub> is Ala, Arg, Asp, Glu, Leu, Phe, Pro, or Thr (preferably Glu or Pro);

X<sub>9</sub> is Ala, Arg, Asn, or Leu (preferably Leu);

25 X<sub>10</sub> is Ile, Leu, Met, Pro, Ser, or Thr (preferably Thr);

X<sub>11</sub> is Ala, Arg, Asn, Gly, His, Lys, Ser, or Tyr;

X<sub>12</sub> is Ala, Arg, Asn, Gln, Leu, Met, Ser, Trp, Tyr, or Val;

X<sub>14</sub> is Asp, Gly, Leu, Phe, Tyr, or Val (preferably Leu);

X<sub>15</sub> is Asn, His, Leu, Pro, or Tyr (preferably His, Leu or Pro); and

30 X<sub>16</sub> is Asn, Asp, His, Phe, Ser, or Tyr, (preferably Asp or Ser);

(6) X<sub>1</sub>-X<sub>2</sub>-X<sub>3</sub>-Cys-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-X<sub>9</sub>-X<sub>10</sub>-X<sub>11</sub>-X<sub>12</sub>-X<sub>13</sub>-X<sub>14</sub>-Cys-X<sub>16</sub>-X<sub>17</sub>-X<sub>18</sub>

(SEQ ID NO:5),

wherein

X<sub>1</sub> is Arg, Asp, Gly, His, Leu, Phe, Pro, Ser, Trp, Tyr, or is absent (preferably Arg);

X<sub>2</sub> is Ala, Arg, Asn, Asp, Gly, Pro, Ser, or is absent (preferably Asn, Asp, Gly, or Pro);

X<sub>3</sub> is Arg, Asn, Gln, Glu, Gly, Lys, Met, Pro, Trp or Val (preferably Gly or Met);

X<sub>5</sub> is Arg, Asn, Gln, Glu, His, Leu, Phe, Pro, Trp, Tyr, or Val (preferably Trp, Tyr, or Val);

X<sub>6</sub> is Arg, Asp, Gln, Gly, Ile, Lys, Phe, Thr, Trp or Tyr (preferably Asp);

X<sub>7</sub> is Ala, Arg, Asp, Glu, Gly, Leu, Ser, or Tyr (preferably Asp);

X<sub>8</sub> is Asp, Gln, Glu, Leu, Met, Phe, Pro, Ser, or Tyr (preferably Leu);

X<sub>9</sub> is Asp, Leu, Pro, Thr, or Val (preferably Leu or Thr);

X<sub>10</sub> is Arg, Gln, His, Ile, Leu, Lys, Met, Phe, Thr, Trp or Tyr (preferably Lys or Thr);

X<sub>11</sub> is Ala, Arg, Asn, Gln, Glu, His, Leu, Lys, Met, or Thr (preferably Arg or Leu);

X<sub>12</sub> is Ala, Asn, Gln, Gly, Leu, Lys, Phe, Pro, Thr, Trp, or Tyr (preferably Thr or Trp);

X<sub>13</sub> is Ala, Arg, Gln, His, Lys, Met, Phe, Pro, Thr, Trp, or Tyr (preferably Met or Phe);

X<sub>14</sub> is Arg, Gln, Glu, Gly, His, Leu, Met, Phe, Pro, Ser, Thr, Tyr, or Val (preferably Val);

X<sub>16</sub> is Arg, Asp, Gly, His, Lys, Met, Phe, Pro, Ser, or Trp (preferably Met);

X<sub>17</sub> is Arg, Asn, Asp, Gly, His, Phe, Pro, Ser, Trp or Tyr, (preferably Arg, His, or Tyr); and

X<sub>18</sub> is Ala, Arg, Asn, Asp, His, Leu, Phe, or Trp (preferably His or Asn);

(7) X<sub>1</sub>-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-X<sub>9</sub>-X<sub>10</sub>-X<sub>11</sub>-X<sub>12</sub> (SEQ ID NO:6),

wherein

X<sub>1</sub> is Ala, Arg, Gly, His, Leu, Lys, Met, Phe, Trp, Tyr, or Val (preferably Gly, Tyr, or Val);

X<sub>2</sub> is Ala, Arg, Gln, His, Ile, Leu, Phe, Thr, Trp, or Tyr (preferably His or Tyr);

X<sub>3</sub> is Ala, Asp, Lys, Phe, Thr, Trp or Tyr (preferably Asp or Tyr);

X<sub>4</sub> is Arg, Asp, Gln, Lys, Met, Phe, Pro, Ser, Tyr, or Val (preferably Asp or Gln);

X<sub>5</sub> is Asp, Leu, Lys, Phe, Pro, Ser, or Val (preferably Leu or Ser);

X<sub>6</sub> is His, Ile, Leu, Pro, Ser, or Thr (preferably Leu or Thr);

X<sub>7</sub> is Arg, Gly, His, Leu, Lys, Met, or Thr (preferably Lys or Thr);

X<sub>8</sub> is Ala, Arg, Asn, Ile, Leu, Lys, Met, or Thr (preferably Leu or Lys);

X<sub>9</sub> is Ala, Asn, Arg, Asp, Glu, Gly, His, Leu, Met, Ser, Trp, Tyr, or Val (preferably Met or Ser);

X<sub>10</sub> is Ile, Leu, Phe, Ser, Thr, Trp, Tyr, or Val (preferably Thr or Leu);

X<sub>11</sub> is Ala, Arg, Gly, His, Ile, Leu, Lys, Pro, Ser, Thr, Trp, Tyr, or Val (preferably Pro or Thr);  
and

X<sub>12</sub> is Arg, Asp, His, Leu, Lys, Met, Phe, Pro, Ser, Trp, Tyr, or Val (preferably Arg or Pro);

(8) X<sub>1</sub>-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-X<sub>9</sub>-X<sub>10</sub>-X<sub>11</sub>-X<sub>12</sub>-X<sub>13</sub> (SEQ ID NO:7),

5 wherein

X<sub>1</sub> is Asp, Gln, Glu, Gly, His, Lys, Met, or Trp (preferably Glu or Lys);

X<sub>2</sub> is Arg, Gln, His, Ile, Leu, or Pro (preferably His or Pro);

X<sub>3</sub> is Asp, Gly, Ile, Lys, Thr, Tyr or Val (preferably Tyr);

X<sub>4</sub> is Asn, Asp, Gln, Glu, Met, Pro, Ser, or Tyr (preferably Asp or Gln);

10 X<sub>5</sub> is Asn, Asp, His, Ile, Leu, Met, Pro, Thr or Val (preferably Asn or Thr);

X<sub>6</sub> is Asp, Glu, His, Leu, Lys, Pro, or Val (preferably Asp or Pro);

X<sub>7</sub> is Arg, Asn, Gln, His, Ile, Leu, Met, Pro, or Thr (preferably Ile or Pro);

X<sub>8</sub> is Gln, Gly, His, Leu, Met, Ser, or Thr (preferably Leu or Thr);

X<sub>9</sub> is Asn, Gln, Gly, His, Leu, Lys, Ser, or Thr (preferably Lys);

5 X<sub>10</sub> is Ala, Gly, Ile, Leu, Lys, Met, or Phe (preferably Gly or Met);

X<sub>11</sub> is Ala, Glu, His, Ile, Leu, Met, Ser, Thr, Trp, Tyr, or Val (preferably Ala or Thr);

X<sub>12</sub> is Arg, Gln, Glu, Gly, His, Ile, Lys, Tyr, or Val (preferably Arg or His); and

X<sub>13</sub> is Arg, Asn, Glu, His, Ile, Ser, Thr, Trp, or Val (preferably His);

(9) Cys-X<sub>2</sub>-Phe-X<sub>4</sub>-Trp-Glu-Cys (SEQ ID NO: 8),

20 wherein

X<sub>2</sub> is Phe, Trp, or Tyr (preferably Tyr); and

X<sub>4</sub> is Pro or Tyr (preferably Pro); or

(10) Cys-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-Cys (SEQ ID NO: 9),

wherein

25 X<sub>2</sub> is Asp, Ile, Leu, or Tyr (preferably Asp or Leu);

X<sub>3</sub> is Arg, Asp, Glu, His, Ile, Leu, Lys, Phe, Pro, Tyr, or Val (preferably Glu or Leu);

X<sub>4</sub> is His, Leu, Lys, or Phe (preferably His or Leu);

X<sub>5</sub> is Leu, Pro, or Thr (preferably Thr or Pro);

X<sub>6</sub> is Arg, Asn, Gly, His, Ile, Lys, Met, or Trp (preferably Lys); and

30 X<sub>7</sub> is Ala, Asn, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Ser, Trp, Tyr, or Val; or

(11) Cys-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-Cys (SEQ ID NO:10),

wherein

X<sub>2</sub> is Asn, Asp, Pro, Ser, or Thr (preferably Asp);

X<sub>3</sub> is Arg, Asp, Ile, Leu, Met, Pro, or Val (preferably Ile);

X<sub>4</sub> is Ala, Ile, Leu, Pro, Thr, or Val (preferably Val or Leu);

5 X<sub>5</sub> is Asn, His, Ile, Leu, Lys, Phe, or Thr (preferably Thr);

X<sub>6</sub> is Asn, Glu, Gly, His, Leu, Lys, Met, Pro, or Thr (preferably Leu);

X<sub>7</sub> is Arg, Asn, Asp, Gln, Glu, Gly, Ile, Lys, Met, Pro, Ser, or Trp;

X<sub>8</sub> is Arg, Glu, Gly, Lys, Phe, Ser, Trp, or Tyr (preferably Ser); or

(12) Cys-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-X<sub>9</sub>-Cys (SEQ ID NO:11),

10 wherein

X<sub>2</sub> is Asp, Gln, His, Ile, Leu, Lys, Met, Phe, or Thr;

X<sub>3</sub> is His, Ile, Leu, Met, Phe, Pro, Trp, or Tyr;

X<sub>4</sub> is Asp, His, Leu, or Ser (preferably Asp);

X<sub>5</sub> is Ala, Arg, Asp, Glu, Leu, Phe, Pro, or Thr (preferably Glu or Pro);

5 X<sub>6</sub> is Ala, Arg, Asn, or Leu (preferably Leu);

X<sub>7</sub> is Ile, Leu, Met, Pro, Ser, or Thr (preferably Thr);

X<sub>8</sub> is Ala, Arg, Asn, Gly, His, Lys, Ser, or Tyr;

X<sub>9</sub> is Ala, Arg, Asn, Gln, Leu, Met, Ser, Trp, Tyr, or Val; or

(13) Cys-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-X<sub>9</sub>-X<sub>10</sub>-X<sub>11</sub>-Cys (SEQ ID NO: 12),

20 wherein

X<sub>2</sub> is Arg, Asn, Gln, Glu, His, Leu, Phe, Pro, Trp, Tyr, or Val (preferably Trp, Tyr, or Val);

X<sub>3</sub> is Arg, Asp, Gln, Gly, Ile, Lys, Phe, Thr, Trp or Tyr (preferably Asp);

X<sub>4</sub> is Ala, Arg, Asp, Glu, Gly, Leu, Ser, or Tyr (preferably Asp);

X<sub>5</sub> is Asp, Gln, Glu, Leu, Met, Phe, Pro, Ser, or Tyr (preferably Leu);

25 X<sub>6</sub> is Asp, Leu, Pro, Thr, or Val (preferably Leu or Thr);

X<sub>7</sub> is Arg, Gln, His, Ile, Leu, Lys, Met, Phe, Thr, Trp or Tyr (preferably Lys or Thr);

X<sub>8</sub> is Ala, Arg, Asn, Gln, Glu, His, Leu, Lys, Met, or Thr (preferably Arg or Leu);

X<sub>9</sub> is Ala, Asn, Gln, Gly, Leu, Lys, Phe, Pro, Thr, Trp, or Tyr (preferably Thr or Trp);

X<sub>10</sub> is Ala, Arg, Gln, His, Lys, Met, Phe, Pro, Thr, Trp, or Tyr (preferably Met or Phe);

30 X<sub>11</sub> is Arg, Gln, Glu, Gly, His, Leu, Met, Phe, Pro, Ser, Thr, Tyr, or Val (preferably Val);

(14) Ala-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-Asp-X<sub>6</sub>-Leu-Thr-X<sub>9</sub>-Leu-X<sub>11</sub>-X<sub>12</sub>-X<sub>13</sub>-X<sub>14</sub> (SEQ ID NO:447),

wherein

X<sub>2</sub> is Asn, Ser, Tyr, Asp, Phe, Ile, Gln, His, Pro, Lys, Leu, Met, Thr, Val, Glu, Ala, Gly, Cys, or Trp (i.e., any amino acid except Arg; preferably Asn);

X<sub>3</sub> is Trp, Glu, Lys, Cys, Leu, Ala, Arg, Gly, or Ser (preferably Trp);

5 X<sub>4</sub> is Tyr, Phe, Glu, Cys, Asn (preferably Tyr);

X<sub>6</sub> is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala (preferably Pro or Ser);

X<sub>9</sub> is Lys, Asn, Gln, Gly, or Arg (preferably Lys);

X<sub>11</sub> is Trp, Ser, Thr, Arg, Cys, Tyr, or Lys (preferably Trp);

X<sub>12</sub> is Leu, Phe, Val, Ile, or His (preferably Leu);

10 X<sub>13</sub> is Pro, Leu, His, Ser, Arg, Asn, Gln, Thr, Val, Ala, Cys, Ile, Phe, or Tyr (i.e., not Asp, Glu, Gly, Lys, Met, or Trp; preferably Pro); and

X<sub>14</sub> is Asp, Glu, Asn, Val, His, Gln, Arg, Gly, Ser, Tyr, Ala, Cys, Lys, Ile, Thr or Leu (i.e., not Phe, Met, Pro, or Trp; preferably Asp); and

(15) X<sub>1</sub>-X<sub>2</sub>-Asp-X<sub>4</sub>-Leu-Thr-X<sub>7</sub>-Leu-X<sub>9</sub>-X<sub>10</sub> (SEQ ID NO:448),

15 wherein

X<sub>1</sub> is Trp, Glu, Lys, Cys, Leu, Ala, Arg, Gly, or Ser (preferably Trp);

X<sub>2</sub> is Tyr, Phe, Glu, Cys, Asn (preferably Tyr);

X<sub>4</sub> is Pro, Ser, Thr, Phe, Leu, Tyr, Cys, or Ala (preferably Pro or Ser);

X<sub>7</sub> is Lys, Asn, Gln, Gly, or Arg (preferably Lys);

20 X<sub>9</sub> is Trp, Ser, Thr, Arg, Cys, Tyr, or Lys (preferably Trp); and

X<sub>10</sub> is Leu, Phe, Val, Ile, or His (preferably Leu).

70. The method according to claim 69, wherein the BLYS binding polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 20-168 and 186-435, as depicted in Tables 1-8 and 13.

71. The method according to claim 69, wherein the BLYS binding polypeptide comprises an amino acid sequence selected from the group consisting of:

Ala-Gly-Lys-Glu-Pro-Cys-Tyr-Phe-Tyr-Trp-Glu-Cys-Ala-Val-Ser-Gly (SEQ ID NO:450);

Ala-Gly-Val-Pro-Phe-Cys-Asp-Leu-Leu-Thr-Lys-His-Cys-Phe-Glu-Ala-Gly (SEQ ID NO:451);

Gly-Ser-Ser-Arg-Leu-Cys-His-Met-Asp-Glu-Leu-Thr-His-Val-Cys-Val-His-Phe-Ala-Pro (SEQ ID NO:452);

Gly-Asp-Gly-Gly-Asn-Cys-Tyr-Thr-Asp-Ser-Leu-Thr-Lys-Leu-His-Phe-Cys-Met-Gly-Asp-Glu (SEQ ID NO:453);

5 Gly-Tyr-Asp-Val-Leu-Thr-Lys-Leu-Tyr-Phe-Val-Pro-Gly-Gly (SEQ ID NO:454);

Trp-Thr-Asp-Ser-Leu-Thr-Gly-Leu-Trp-Phe-Pro-Asp-Gly-Gly (SEQ ID NO:455);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:186);

Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:456);

Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu (SEQ ID NO:457);

10 Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Val (SEQ ID NO:189);

Ala-Asn-Trp-Phe-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:309);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Ser-Leu-Pro-Asp (SEQ ID NO:458);

Ala-Asn-Trp-Tyr-Asp-Pro-Leu-Thr-Lys-Leu-Trp-Phe-Pro-Asp (SEQ ID NO:353);

Ala-Asn-Trp-Tyr-Asp-Ser-Leu-Thr-Lys-Leu-Trp-Leu-Pro-Asp (SEQ ID NO:327).